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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
MOORE, WILLIAM W

ART UNIT	PAPER NUMBER
1652	9

DATE MAILED: 01/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/498,305	Applicant(s) ENSLEY, BURT D.	
	Examiner William W. Moore	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,9-15 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,9-15 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

Applicant's Amendment A, Paper No. 8 filed October 19, 2001, has been entered and claims 4, 6-8, 16, and 18-25 were canceled at Applicant's request, overcoming the rejection of record of claims herein for lack of an adequate written description under the first paragraph of 35 U.S.C. §112. Amendments to claims 1 and 12 overcome the objection of record to these claims and the rejection of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 5, 9-13 and 15 are for reasons of record rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for a methods utilizing an unaltered native, or recombinantly-produced, exogenous or endogenous, lysyl oxidase and utilizing a native, exogenous or endogenous tropoelastin as well as recombinantly-produced tropoelastin isoforms having amino acid sequences encoded by exons of the human and bovine tropoelastin genes, and for kits comprising same,

does not reasonably provide enablement for methods of promoting wound healing utilizing a truncated lysyl oxidase or a lysyl oxidase having amino acid sequence alterations, or kits comprising same, or for methods utilizing a tropoelastin having an amino acid sequence that differs from that encoded by the exons of the human and bovine tropoelastin genes by one or more amino acid substitutions, deletions and insertions, or combinations thereof, at regions encoded by internal regions of exons, or kits comprising same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The amendments of Paper No. 8 to claims 1 and 13 overcome in part the rejection of record. Applicant's arguments filed October 19, 2001, addressing the other enablement issue of record concerning the nature of the enzyme and substrate products to be used in a claimed method, or included in a claimed kit, have been fully considered but they are not persuasive. The amendment to claims 1 and 15 to include the limitation "substantially identical to wild type" modifying the enzyme, lysyl oxidase, and its substrate, tropoelastin

does not alter the scope of the term "modified" in claims 3 and 15 which, absent recitation of a specific, disclosed and enabled modificati on, must be construed according to the discussions at pages 10, 12 and 13 of the specification. Claims 1, 5 and 9-13 are therefore included in this rejection because they must include the subject matters of modified substrates and/or enzymes of claims 3 and 15, depending from claims 1 and 13. Claims 1, 3, 13 and 15 thus contemplate arbitrary assignment of amino acid substitutions, additions or deletions in a tropoelastin substrate or a lysyl oxidase enzyme. Neither the specification nor the prior art supports modification of any portion of the amino acid sequences of native lysyl oxidases, nor any insertions, deletions, or substitutions anywhere, in any combination or any pattern, in amino acid sequences of tropoelastins other than those resulting from alternative splicing among and within exons or produced by selective exon deletion. The prior art made of record herewith is evidence, see, e.g. Parks et al., that no teaching in the relevant arts of protein engineering and molecular biology can be combined with the specification's disclosure to support the contemplated alteration of tropoelastin and lysyl oxidase acid sequences. Mere sequence perturbation cannot enable the design and preparation of nucleotide sequences encoding a myriad of divergent tropoelastins and lysyl oxidases yet provide the public with nucleotide sequences encoding either a substrate or an enzyme that retains its native function.

It is well settled that 35 U.S.C. §112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (recognizing and applying the "*Forman*" factors). Cf., *Ex parte Forman*, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986) (citing eight factors relevant to analysis of

enablement). The standard set by the CCPA is not to "make and screen" any and all possible alterations because a reasonable correlation must exist between the scope asserted in the claimed subject matter and the scope of guidance the specification provides. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (scope of enablement varies inversely with degree of unpredictability of factors involved in physiological activity of small peptide hormone); see also, *Ex parte Maizel*, 27 USPQ2d 1662, 1665 (Bd. Pat. App. & Int. 1992) (equivalency of divergent gene products unsupported where only a single B-cell growth factor allele disclosed). The Federal Circuit approved the CCPA's standard in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997).

The Federal Circuit has also considered whether definitional statements might enable a claim scope argued to extend beyond a disclosed gene product having its native amino acid sequence to embrace a specific variant gene product encoded by a specifically-altered DNA sequence. *Genentech, Inc. v. The Wellcome Found. Ltd.*, 29 F.3d 1555, 31 USPQ2d 1161 (Fed. Cir. 1994). The court held that only a narrow structural and functional definition was enabling precisely because the sweeping definitions of scope in the patent specification could not reasonably have been relied upon by the PTO in issuing the patent. *Genentech*, 29 F.3d 15 at 1564-65, 31 USPQ2d at 1168. Applying the "*Forman*" factors discussed in *Wands*, ***supra***, to Applicant's disclosure, it is apparent that :

a) the specification lacks adequate, specific, guidance for altering DNA sequences coding for, and encoded amino acid sequences of, a native lysyl oxidase or the exon-encoded amino acid sequences specified by tropoelastin genes,

b) the specification lacks working examples wherein DNA sequences coding for, and encoded amino acid sequences of, a native lysyl oxidase or the exon-encoded amino acid sequences specified by tropoelastin genes, are altered,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such alteration, and,

d) unpredictability exists in the art where no lysyl oxidases, or internal regions or tropoelastins specified by exons of tropoelastin genes, have yet been identified for concurrent modification.

Thus the broad scope of the subject matters embraced by the term "modified" is considered to be unsupported by the present specification, even if taken in combination with the teachings available in the prior art. This rejection may be overcome as to claims 1, 5 and 9-13 by canceling claims 3 and 15.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 5, 9-14 and 17 rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over Weiss, WO 98/06830.

Weiss discloses, see pages 25-29, 31 and 32 and claims 39-53, the preparation of pharmaceutical compositions comprising a human or other mammalian lysyl oxidase and pharmaceutical compositions comprising a human or other mammalian tropoelastin for joint application to a wound to promote healing. While Weiss discusses modification of the amino acid sequence of, at least, lysyl oxidase, none are disclosed or enabled thus claims 3 and 15 are not included in this rejection. Claims 39-41, 46, 47 and 51 of Weiss all permit separate application to a wound to promote healing of compositions that separately comprise the enzyme and a tropoelastin substrate, where a vial is considered to be a component of a kit, anticipating the methods and kits of claims 1, 2, 5, 9-14 and 17. In the alternative, the disclosure of Weiss is considered to have rendered the subject matters of claims 1, 2, 5, 9-14 and 17 obvious to one of ordinary skill in the art at the time the

invention was made because such an artisan at that time would have reasonably considered the disclosure and claims of Weiss to teach that separate administration of both the enzyme and its tropoelastin substrate to a wound to promote healing may occur sequentially, simultaneously, or repeatedly, and that such an artisan would have considered the further teachings of mechanical methods of approximating wound surfaces such as those suggested at page 32 of Weiss to suggested the use of further methods such as those recited in claim 10 herein and application devices such as that of claim 11 herein.

Conclusion

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on September 10, 2001 prompted the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 703.308.0583. The examiner can normally be reached between 7:00AM-5:30PM EST on Mondays and Wednesdays, between 7:00AM-1:30PM EST on Tuesdays and Thursdays, and between 8:30AM and 5:00PM EST on Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached at 703.308.3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703.308.4242 for regular communications and 703.308.0294 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703.308.0196.

William W. Moore
December 31, 2001

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